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HOWARD, ZACHARY C	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/772,090	BARON ET AL.	
	Examiner	Art Unit	
	Zachary C. Howard	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43 and 57-68* is/are pending in the application.

4a) Of the above claim(s) *1-42,61 and 67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43,57-60,62-66 and 68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-43 and 57-68* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

Applicants' response filed 10/22/07 has been entered. Applicants provide a new listing of the claims that does not amend any of the claims in the listing filed 7/3/07.

Claims 1-43 and 57-68 are pending.

Claims 1-42 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicants timely traversed the restriction (election) requirement in the reply filed on 1/8/07.

In the Office Action mailed 9/20/07 Applicants were required to elect a single species of "enhanced vascular growth". Applicants' election of "enhanced vascular growth accompanying a solid tumor" in the reply filed on 10/22/07 is acknowledged.

Claims 61 and 67 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

Claims 43, 57-60, 62-66 and 68 are under consideration, as they read upon the elected species.

Information Disclosure Statement

The Information Disclosure Statement of 10/22/07 has been considered.

Withdrawn Objections and/or Rejections

The objection to the specification at pg 3-4 of the 4/5/07 Office Action is *withdrawn* in view of Applicants' amendments to the specification.

Maintained Objections and/or Rejections

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43, 57-60, 62-66 and 68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection was set forth at pg 4-12 of the 4/5/07 Office Action for claim 43; new claims 57-60, 62-66 and 68 are herewith included.

Applicants' arguments (10/2207; pg 14-17) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

It is first noted that the elected species under consideration is "enhanced vascular growth accompanying a solid tumor" and that because this species is not allowable (for the reasons set forth previously and maintained herein), the other recited species (ocular neovascularization) has not been considered.

In the response, Applicants argue that the specification and the art provide extensive guidance concerning both "the structural and functional characteristics of the compounds for use in the claimed methods" and "vasculogenesis and angiogenesis", such that one of skill could practice the claimed invention without undue experimentation. Applicants further argue that "the state of the art since the effective filing date of the instant application supports Applicants' contention that the claimed invention is enabled throughout its scope based on the specification and level of skill in the art" (pg 14). Applicants point to examples from the relevant art, including Pola et al #1 (2001), Pola et al #2 (2003), Heiser et al (2004) Byrd et al (2004), and Surace et al(2006) (Exhibits 1-5). Applicants argue that these articles provide support for the use

of agents that inhibit hedgehog signaling (e.g., hedgehog antagonists) for inhibiting vasculogenesis and angiogenesis.

Applicants' arguments have been fully considered but are not found persuasive. It is maintained for the reasons set forth previously that the practicing the claimed methods would require undue experimentation. It is noted that Applicants have not made the full text of each article available for review by the Examiner; only abstracts have been provided. Therefore, it is assumed that Applicants are relying solely on the teachings in the abstracts in support of their arguments. Furthermore, the elected species of "abnormally enhanced vascular growth" under consideration is "enhanced vascular growth accompanying a solid tumor" and the abstracts of Pola et al #1 (2001), Pola et al #2 (2003), Byrd et al (2004), and Surace et al(2006) do not concern the elected species. With respect to the abstract of Heiser et al (2004), this abstract merely indicates that hedgehog signaling can be involved in pancreatic cancer. The Examiner does not dispute that the relevant post-filing date art teaches that hedgehog signaling may be involved in some cancers. However, as set forth in the previous Office Action, "abnormal vascular growth in adult subjects does not necessarily involve expression of the same molecules in different conditions". This statement applies to the newly elected species, as the relevant post-filing date art teaches variability in whether or not (and if so, how) the hedgehog pathway is activated in cancer. For example, Thievessen et al (2005) teaches, "our data suggest that hedgehog pathway is weakly active in normal adult urothelial cells and of limited importance in TCC [transitional cell carcinoma]" (abstract) and "the hedgehog pathway has been reported to become activated in small cell lung cancer, but not in other histological types of lung cancer" (pg 376 of Thievessen et al, 2005. Journal of Cellular Physiology. 203: 372-377). Furthermore, Thievessen teaches variability in the mechanism of hedgehog pathway induction in various types of cancer: "constitutive activation of the hedgehog pathway in basal cell carcinoma and medullablastoma is caused by different genetic alterations including inactivation of *PTCH1* and *SUFU* genes as well as point mutations activating *SMO* ... since the pathway is not completely known, however, alterations in further components

cannot be excluded. Recently, a second mechanism leading to hedgehog pathway activation has been observed in small cell lung cancer ... and in some gastrointestinal cancer cell lines ... In these cancers, an autocrine loop may be initiated by SHH overexpression" (pg 372). The instant specification provides no guidance as to how to select particular hedgehog antagonists to treat particular types of cancer. Instead, the instant specification broadly teaches treatment of any type of tumor with any type of hedgehog antagonist. However, many of the potential antagonists may not work with many types of tumors. For example, new claim 57 encompasses use of a "hedgehog antibody" to treat any type of tumor. Such an antagonist would not work with a tumor in which hedgehog signaling is not involved. Furthermore, a hedgehog antibody may not inhibit hedgehog signaling in a cancer cell in which the hedgehog receptor (the patched protein) inactivation causes pathway overexpression. Wang et al (2007) teach "Inactivating mutations in *Ptch1* are the most frequent cause of Hh-related tumors" (pg 163 of Wang et al, 2007. Current Opinion in Cell Biology. 19: 159-165). In order to practice the claimed method, the skilled artisan would first need to make and test a wide range of hedgehog antagonists for the ability to treat a variety of hedgehog-independent and hedgehog-dependent tumors.

Applicants further argue that the amended claims obviate the following issues raised in the 4/5/07 Office Action: the breadth of the phrase "enhanced vascular growth" (pg 5-6); the breadth of "hedgehog compounds" for use in the claimed methods (pg 6-8); treatment of diseases wherein inhibition of angiogenesis is contrary to treatment of the disease (pg 8); and the breadth of a "hedgehog compound capable of inhibiting the activity of a gene product expressed in an extraembryonic tissue" (pg 8-12).

Applicants' arguments have been fully considered but are not found persuasive. Applicants have introduced new dependent claims directed specific species of enhanced vascular growth but the independent claims (amended claim 43 and new claim 65) are still directed to treatment of the same scope of "enhanced vascular growth in a subject" as claimed previously. Applicants have narrowed claim 43 to a method of use of "a hedgehog compound" that is "a hedgehog antagonist capable of inhibiting

hedgehog signaling" and introduced new claim 65 directed to "means for inhibiting hedgehog signaling". Such recitations now exclude compounds capable of inhibiting gene products other than hedgehog expressed in extraembryonic tissue. However, the previous rejection also set forth reasons on pg 8-12 why the claims lacked enablement even if the "the gene product to be inhibited is Sonic hedgehog". Therefore, the rejection of the claims is maintained for the reasons set forth previously and reiterated herein. Furthermore, the reasons for the lack of enablement for the claimed method as practiced with respect to the newly recited elected species (enhanced vascular growth accompanying a solid tumor) are addressed above.

Applicants further argue that the Office Action "appears to hinge enablement solely on predictability". Applicants argue that "the knowledge and technology available at the time of filing, permitted the preparation and testing of hedgehog antagonists, for example, blocking antibodies and variant polypeptides". Applicants argue that the methods for making such antagonists were completely routine and the specification provided numerous in vitro models for testing whether particular compounds functioned as inhibitors of hedgehog activity". Applicants point to the Examples in the specification. Applicants argue that any invitation to experiment is routine rather than undue.

Applicants' arguments have been fully considered but are not found persuasive. The rejection under 35 USC 112, first paragraph for lack of enablement did not hinge solely on predictability. Instead, the eight *Wands* factors enumerated on page 5 of the 4/5/07 Office Action were fully considered; the "level of predictability in the art" is only one of the eight factors. It is true that the skilled artisan at the time of filing a screening assay existed for testing for the ability of a compound to antagonize hedgehog signaling. However, the claims are not directed to a method of screening for an antagonist of hedgehog signaling. Instead, the claims are directed to a method of treatment using a genus of structurally undefined hedgehog signaling antagonists, the identification of which requires screening of a vast genus of compounds to identify those compounds in the genus, prior to even testing them for the ability to function in the claimed treatment method. Applicants provide a single example of a hedgehog signaling

antagonist (a Shh blocking antibody) and no examples of an antagonist that can function in the claimed method for even a single species of tumor. Furthermore, Applicants provide no arguments in response to the lack of enablement for administration of compounds (e.g., protein or gene therapy) as set forth at pg 10-12 of the 4/5/07 Office Action. It is maintained that the specification fails to teach the skilled artisan how to use the hedgehog compounds as a therapeutic reagent without resorting to undue experimentation. The specification has not provided the person of ordinary skill in the art the guidance necessary to be able to use the claimed method for the above stated purpose. Due to the large quantity of experimentation necessary to determine how to make and use a hedgehog signaling inhibitor for treatment of abnormally enhanced vascular growth, the lack of direction/guidance presented in the specification regarding same, lack of working examples and the teachings of the prior art and the complex nature of the invention, undue experimentation would be required of the skilled artisan to use the claimed invention. What Applicants have provided is a mere wish or plan and an invitation to experiment.

Claim Rejections - 35 USC § 112, 1st paragraph, written description

Claims 43, 57-60, 62-66 and 68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection was set forth at pg 12-15 of the 4/5/07 Office Action for claim 43; new claims 57-60, 62-66 and 68 are herewith added.

Applicants' arguments (10/22/07; pg 17-18) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response, Applicants argue that the cases cited in the rejection (including *Fiers v. Revel*, *Amgen Inc. v. Chugai*, and *Fiddes v. Baird*) concerned protein and nucleic acid product claims rather than method claims. Applicants argue that the written

description requirement requires conceptual rather than physical possession. Applicants argue that "While *Amgen v. Chugai* stands for the proposition that a nucleic acid is not conceived until the sequence is known, case law does not support the extension of this holding to method claims such as those presented by Applicants. Applicants are not aware of, nor does the Office Action cite, any case holding that a method is not conceived until reduction to practice occurs". Applicants argue that methods are "not subject to the doctrine of simultaneous conception and reduction to practice that applies when nucleic acids and proteins are claimed as compositions of matter. Instead, methods ... can be conceived independently and are constructively reduced to practice, at the very least, by the filing of a patent application" and "the specification as filed fully supports Applicants' conception of the subject matter of the pending claims at the time of filing of the present application as required by 35 U.S.C. § 112, first paragraph".

Applicants' arguments have been fully considered but are not found persuasive. It is maintained that the decisions cited previously (*Vas-Cath*, *Fiers v. Revel*, *Amgen Inc v Chugai Pharmaceutical and Fiddes v.* Baird) are as applicable to claims reciting methods of use of products as they are to the products themselves. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed" (pg 1117). As set forth previously, the claims are genus claims because the claims are directed to a method of using a potentially vast genus of structurally undefined compounds. Practicing a method of use of a genus of compounds requires possession of the genus of compounds to be used in the method. The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of compounds to be used in the method, and therefore conception is not achieved until reduction to practice of the genus of compounds has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See

Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Consistent with *Fiddes*, said genus of "mammalian FGFs" would not have written description merely because said genus was recited in a method of use rather than in a product claim.

Applicants further argue that new claims 64-68 are "means-plus-function claims". Applicants argue "it is difficult to envision a set of circumstances under which it would be appropriate to reject means-plus-function claims as lacking sufficient written description" (pg 18). Applicants argue that claims interpreted under 35 USC 112, 6th paragraph "are construed to cover the corresponding structure, material, or acts described in the specification and equivalents thereof" and "are so intimately tied to the disclosure ... that the claims by definition must be adequately described". Applicants point to MPEP 2182 as stating that "the specification need not describe the equivalents of the structures, material, or acts corresponding to the means- (or step-) plus-function claims".

Applicants' arguments have been fully considered but are not found persuasive. MPEP 2181.II states, "the invocation of 35 U.S.C. 112, sixth paragraph, does not exempt an applicant from compliance with 35 U.S.C. 112, first and second paragraphs. See *Donaldson*, 16 F.3d at 1195, 29 USPQ2d at 1850; *Knowlton*, 481 F.2d at 1366, 178 USPQ at 493." In the instant case, the disclosure (specification) lacks a written description of the full scope of "means for inhibiting hedgehog signaling". The specification discloses a single specific structure that can inhibit hedgehog signaling - a Sonic hedgehog blocking antibody that can inhibit the hedgehog signaling pathway by binding to the hedgehog receptor. However, as set forth previously, the specification teaches that a vast genus of compounds, including hedgehog variants, other polypeptides, nucleic acids and other structurally unrelated compounds are potentially hedgehog inhibitors. These unknown compounds are not equivalents of the structure of the Sonic hedgehog blocking antibody because they each function to inhibit the

hedgehog pathway in a different manner than the hedgehog antibody. The hedgehog pathway consists of multiple extracellular (e.g., hedgehog proteins), transmembrane (e.g., patched, smoothened), and intracellular components (e.g., gli), and inhibition of hedgehog signaling can occur through interaction of an antagonist with any component of the pathway. The claims are "single means claims". As set forth in MPEP 2164.08(a), "[w]hen claims depend on a recited property, a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor."

Therefore, it is maintained that only a method of using a hedgehog compound that is a SHH blocking antibody, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

New rejections necessitated by Applicants' amendment

Claim Rejections - 35 USC § 112, 1st paragraph, new matter

Claims 43, 57-60, 62-66 and 68 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because the claims contain new matter.

Claim 43 was amended on 7/3/07 to limit the hedgehog compound used in the claimed method to "a hedgehog antagonist capable of inhibiting hedgehog signaling". The response filed on 7/3/07 indicates that support for this amendment can be found in paragraphs 42, 53 and 118 of the published application. Paragraph 42 teaches only a definition of "vascular growth". Paragraph 118 teaches only species of excess vascularization that can be inhibited by methods of the invention. Paragraph 53 teaches a definition of "hedgehog compound" that includes "antagonists of hedgehog protein receptors" but not "a hedgehog antagonists capable of inhibiting hedgehog signaling". The scope of the compounds encompassed by these two types of antagonists is different because an antagonist that is capable of inhibiting hedgehog signaling is not necessarily an antagonist of a hedgehog protein receptor. Furthermore, the teachings of

the entire specification have been reviewed and there is no conception of the specific genus of "hedgehog antagonists capable of inhibiting hedgehog signaling". Therefore, the specification as originally filed lacks support for the genus of molecules used in the methods of the amended claims. Claims 58 and 60 are included in this rejection because they each depend from claim 64 and encompass the same new matter.

New claim 57 depends from amended claim 43 and limits the hedgehog compound to "a hedgehog antibody". The response filed on 7/3/07 indicates that support for this new claim can be found in paragraphs 42, 53 and 118 of the published application. Paragraph 42 teaches only a definition of "vascular growth". Paragraph 118 teaches only species of excess vascularization that can be inhibited by methods of the invention. Paragraph 53 teaches a definition of "hedgehog compound" that includes "antagonists of hedgehog protein receptors" but not "a hedgehog antibody" that is "a hedgehog antagonist capable of inhibiting hedgehog signaling". Furthermore, the teachings of the entire specification have been reviewed and there is no conception of the specific genus of "hedgehog antibody" that is "a hedgehog antagonist capable of inhibiting hedgehog signaling". The term "hedgehog antibody" as used in the new claim is not defined in the specification and potentially includes both antibodies that bind to hedgehog proteins as well as other antibodies that interact with the hedgehog pathway. The specification as originally filed lacks support for the genus of molecules used in the methods of the new claim. Claims 59, 62 and 63 are included in this rejection because they each depend from claim 57 and encompass the same new matter.

New claim 58 also contains new matter for the following reason. The preamble of new claim 58 includes the recitation "a method of inhibiting angiogenesis". Nowhere in the specification is described a specific method of inhibiting angiogenesis. The specification defines "vascular growth" as at least one of vasculogenesis and angiogenesis and includes formation of capillaries, arteries, veins or lymphatic vessels" ([0042]). However, this definition does not provide support for the specific method of inhibiting angiogenesis. While the specification teaches inhibition of "vascular growth" (e.g., [0096]) this term is broader than angiogenesis and does not provide support for

the specific inhibition of angiogenesis. New claims 59 and 65 also contain new matter for this same reason.

New claim 60 also contains new matter for the following reason. New claim 60 recites "the enhanced vascular growth accompanies a solid tumor". However, the specification only teaches "methods are provided for inhibiting vascular growth in subjects suffering from an excess of vascularization or neovascularization as found in, for example, a variety of solid tumors..." Enhanced vascular growth accompanying a solid tumor is different in scope from excess of vascularization or neovascularization in a tumor, as the claim includes growth anywhere in the body that "accompanies" the tumor, but the specification only teaches methods of treating excess or neo-vascularization found in the solid tumor. New claims 62, 63, 66 and 68 also contain new matter for this same reason.

New claim 64 recites a method using "means for inhibiting hedgehog signaling". The response filed on 7/3/07 indicates that support for this new claim can be found in paragraphs 42, 53 and 118 of the published application. Paragraph 42 teaches only a definition of "vascular growth". Paragraph 118 teaches only species of excess vascularization that can be inhibited by methods of the invention. Paragraph 53 teaches a definition of "hedgehog compound" that includes "antagonists of hedgehog protein receptors" but not "means for inhibiting hedgehog signaling". The scope of the compounds encompassed by these two types of antagonists is different because an antagonist that is capable of inhibiting hedgehog signaling is not necessarily an antagonist of a hedgehog protein receptor. Furthermore, the teachings of the entire specification have been reviewed and there is no conception of the specific genus of "means for inhibiting hedgehog signaling". Therefore, the specification as originally filed lacks support for the genus of molecules used in the methods of the new claim. Claims 65, 66 and 68 are included in this rejection because they each depend from claim 64 and encompass the same new matter.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 64-66 and 68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

New claim 64 recites "means for inhibiting hedgehog signaling". As taught in MPEP 2181.II " "If one employs means plus function language in a claim, one must set forth in the specification an adequate disclosure showing what is meant by that language. If an applicant fails to set forth an adequate disclosure, the applicant has in effect failed to particularly point out and distinctly claim the invention as required by the second paragraph of section 112." *In re Donaldson Co.*, 16 F.3d 1189, 1195, 29 USPQ2d 1845, 1850 (Fed. Cir. 1994) (in banc)." In the instant case, Applicants have employed means plus function language in a claim, but do not set forth in the specification an adequate disclosure showing what is meant by that language. The instant specification does not provide a definition of the phrase "means for inhibiting hedgehog signaling". Furthermore, the hedgehog pathway has multiple points of regulation, including extracellular (e.g., hedgehog proteins), transmembrane (e.g., patched, smoothened), and intracellular components (e.g., gli), that can each be inhibited by one or more structurally distinct compounds. Therefore, the disclosure in the specification fails to set forth an adequate disclosure of what is meant by "means for inhibiting hedgehog signaling".

The remaining claims are rejected for depending from an indefinite claim.

Conclusion

No claims are allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

zch

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646